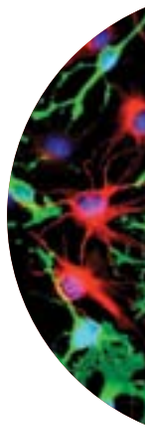

EPIDERMOLYSIS BULLOSA

AN INFANT'S SKIN PEELS OFF IN SHEETS, REVEALING ANGRY RED FLESH BELOW.

In the disease called dystrophic epidermolysis bullosa, there is something wrong with the collagen tethers that anchor the top layer of skin to the dermis beneath. The skin sloughs off or blisters at the slightest insult—the rub of a shirt collar, the touch of a hand, the movement of the eye during dreams. Even birth. • The skin's impermanence results from a misstep in a gene that forms the collagen tethers. • EB comes in a less severe dominant form or a more devastating recessive form. Four to eight babies in the United States are born each year with this latter form. Forty percent will die before age 35, said Alfred Lane, M.D., chair of dermatology and pediatrics at the Stanford University School of Medicine. But even the 24 to 28 children born annually with the dominant form of EB suffer from fragile skin, painful wounds, frequent blisters and scarring. • A team of Stanford University researchers hopes to grow new, genetically corrected skin for these children. Skin that stays where it belongs.

Key to the strategy are induced pluripotent stem cells, grown-up cells that are convinced to return to their embryonic youth. Cells of the embryo may mature into any cell type; that is, they're pluripotent. With induced pluripotency, investigators will take a patient's fully differentiated skin cells and coax them back to pluripotence, says Marius Wernig, M.D., an assistant professor at the Institute for Stem Cell Biology and Regenerative Medicine at Stanford.

While the cells are in their pluripotent state, researchers will repair the gene using homologous recombination. The correction takes advantage of DNA's willingness to swap genetic material with complementary—that is, homologous—DNA strands. The complementary strands introduced to the pluripotent cells will carry a correction for the error that causes EB. Although as few as 1 percent of the cells may adopt the correction, that's enough. Cells identified with properly correct genomes will be grown into skin cells for transplant to patients.

"If you look at this entire project, every step is, in principle, established. In principle we know how we can do it," Wernig said. "The challenge is to pull all the pieces together in a way that works reliably."

WHAT IS IT LIKE TO LIVE WITH EB?

Chuck and Christine Anderson were butterfly children. • Born with an inherited condition that made their skin as fragile as a butterfly wing, Chuck died at 27 of skin cancer. His sister, Christine, died of heart failure at 14. • "These children taught me an incredible lesson in resilience, determination and good cheer," says their mother, Lynn Anderson. She is the president and founder of the Epidermolysis Bullosa Research Foundation.

They were born with the recessive form of dystrophic epidermolysis bullosa. "The glue that holds the skin together is missing," Anderson explains. "The skin tears or blisters at the slightest provocation."

Things as simple as putting on a shoe can cause chronic wounds. "Stiff pants make blisters. Pull on the arm, and the skin comes off," she says.

"Imagine not being able to swallow because you have scarring in your esophagus. You have difficulty eating because you have sores in your mouth," she says. The disease brings chronic anemia, malnutrition and growth retardation because most nutrition goes toward skin repair. When Chuck Anderson was 27, he weighed 59 pounds.

Anderson says she has great hopes for EB research. She is grateful for the researchers "who have helped my children's suffering come to something good, who have helped me believe that EB is not forever."

> "These children taught me an incredible lesson in resilience, determination and good cheer."
> LYNN ANDERSON